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IFW 4-23-04 $DAC


PATENT
Attorney Matter No. 468268-00019
Attorney Docket No. A-65353-6/RMS/RMK

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

| | |
|---|---|
| In re application of | Group No. 1637 |
| MAYO, *et al.* | Examiner: Y. J. Kim |
| Serial No.: 09/812,034 | |
| Filed: March 19, 2001 | Express Mail No. EV 298967462 US |
| For: *Apparatus and Method for Automated Protein Design* | |

**PETITION FOR REVIVAL OF AN APPLICATION FOR PATENT ABANDONED UNINTENTIONALLY UNDER 37 CFR §1.137(b)**

Mail Stop Petition
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Applicants hereby petition for the revival of the above-identified patent application which was unintentionally abandoned under 37 CFR §1.137(b).

1. This application became abandoned on April 15, 2004 for failure to submit the necessary fees and a Notice of Appeal, in Response to the third Advisory Action mailed April 9, 2004 and the Final Office Action mailed October 15, 2004.

2. The entire delay in responding to the Final Office Action mailed October 15, 2003 and due April 15, 2004 until the filing of a grantable petition under 37 CFR 1.37(b)(3) was unintentional. Copies of the Advisory Action mailed April 9, 2004 and the Response to the Advisory Action, transmitted April 14, 2004 are enclosed herewith.



04/26/2004 SDIRETA1 00000033 09812034
01 FC:2453 665.00 OP

3. A Notice of Appeal, a Petition for a Three Month Extension of Time and Fee(s) Due, and a check for $585, which includes $165 for the Notice of Appeal and $420 for a Three Month Extension of Time, is enclosed herewith. Applicants would like to call attention to the fact, that in the Response to Office Action dated February 12, 2004, Applicant submitted authorization to charge $55 for a one-month extension of time to Deposit Account No. 502325 pursuant to 37 C.F.R. 1.17(a). Accordingly, Applicants submit that the total fees due for the Three Month Extension of Time is $475.00 - $55.00 = $420.00. A copy of Response dated February 12, 2004 and the authorization to charge the first month extension fee is enclosed herewith.

4. Also enclosed is a check in the amount of $665 for the fee required under 37 CFR 1.17(m).

5. A terminal disclaimer is not required since this application was filed on or after June 8, 1995.

6. While no further fees are believed due, the Commissioner is hereby authorized to charge any additional fees that may be required including extension fees or any other relief that may be required, or credit any overpayment to Deposit Account Number 50-2319 (Order No. 468268-00019 /A-65353-6/RMS/RMK).

The PTO did not receive the following listed item(s) Check # 585.00 But # 420.00 and # 665.00

Please direct further questions in connection with this Application to the undersigned at (415) 781-1989.

Respectfully submitted,
DORSEY & WHITNEY LLP

By: _____

Dated: 4/21/04

Renee M. Kosslak, Reg. No. 47,717
Robin M. Silva, Reg. No. 38,304
Filed under 37 C.F.R. § 1.34(a)

Four Embarcadero Center
Suite 3400
San Francisco, California 94111-4187
Telephone: (415) 781-1989
Fax No. (415) 398-3249

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/812,034 | 03/19/2001 | Stephen L. Mayo | A-65353-6/RFT/RMS/RMK | 3845 |

7590 04/09/2004

| EXAMINER | |
|---|---|
| KIM, YOUNG J | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1637 | |

DATE MAILED: 04/09/2004

Robin M. Silva, Esq.
DORSEY & WHITNEY LLP
Four Embarcadero Center Suite 3400
San Francisco, CA 94111-4187



File A-65353-006 Atty RFT/RMK/RMS

Due Date 4-15-2004

Type Final Resp / Notice of Appeal Refs

Please find below and/or attached an Office communication concerning this application or proceeding.

| Advisory Action | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/812,034 | MAYO ET AL. | |
| | Examiner | Art Unit | |
| | Young J. Kim | 1637 | |



*--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

THE REPLY FILED FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☐ The a)☐ affidavit, b)☐ exhibit, or c)☐ request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☐ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: _____.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)( PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Continuation of 2. NOTE: If the Amendment were to be entered, claims 65 and 66 would be objected uncer 37 CFR 1.75(c) as being in improper multiple dependent form. The multiple dependent claims 65 and 66 depend from another set of multiple dependent claims 61 and 65, respectively. A multiple dependent claim cannot serve as a basis for another multiple dependent claim because it result in the confusion of claim dependencies.

4-7-04

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

4/8/04


PATENT
Attorney Docket No. A-65353-6/RFT/RMS/RMK
Attorney File No. 468268-00019

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

MAYO, *et al.*

Serial No. 09/812,034

Filed: March 19, 2001

For: *Apparatus and Method for Automated Protein Design*

Group No. 1637

Examiner: Y. J. Kim

*Certificate of Facsimile Transmission*

I certify that this correspondence, included listed enclosures, is being facsimile transmitted to the United States Patent and Trademark Office, Fax No. (703) 872-9306 on April 14, 2004.

Signed: Jessica Newlin
Jessica L. Newlin

**AMENDMENT AND RESPONSE TO ADVISORY ACTION**

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This paper is being submitted in response to the Advisory Action mailed April 9, 2004. The response is filed on or before April 15, 2004, making this a timely filed response. Although no fees are believed to be due at this time, the Commissioner is authorized to charge any additional fees, such as extension fees or other relief, that may be required, or credit any overpayment to Deposit Account No. 50-2319 (Our Order No. A-65353-6/(468268-19)/RMS/RMK).

**Amendments to the Claims** begin on page 2.

**Remarks/Arguments** begin on page 7.

1137133_1

**Amendments to the Claims**

This listing of claims will replace all prior versions and listings of all claims in the application.

Claims 1 -29 (Canceled)

30. (Previously presented) A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

(A) receiving a protein structure of a desired target protein, said protein structure comprising:;

i) a protein template structure comprising a protein backbone structure and at least one non-variable residue; and

ii) a plurality of variable residue positions;

(B) altering at least one supersecondary structure parameter value of said protein backbone structure of said protein;

(C) establishing a group of potential amino acid side chains for a plurality of said variable residue positions of said protein; and

(D) analyzing the interaction of all or part of each of said potential amino acid side chains from said group with all or part of the remainder of said protein structure to generate a set of optimized proteins sequences.

31. (Currently amended) A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

(A) receiving a protein structure of a desired target protein, said protein structure comprising:

i) a protein template structure comprising a protein backbone structure and at least one non-variable residue; and

ii) a plurality of variable residue positions;

(B) altering at least one supersecondary structure parameter value of said protein backbone structure;

(C) classifying each variable residue position as either a core, surface or boundary residue;

(D) establishing a group of potential amino acid side chains for each of said variable residue positions; and

(E) analyzing the interaction of all or part of each of said amino acid side chains from said group with all or part of [[of]] said protein structure to generate a set of optimized protein sequences.

Claims 32-52 (Canceled)

53. (Previously presented) A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

(A) receiving a protein structure of a desired target protein, said protein structure comprising:

i) a protein template structure comprising a protein backbone structure and at least one non-variable residue; and

ii) a plurality of variable residue positions;

(B) altering at least one supersecondary structure parameter value of said protein backbone structure prior to establishing a group of potential amino acid side chains;

(C) establishing a group of potential amino acid side chains for each of said variable residue positions, wherein a first group for a first variable position has a first set of at least two amino acid side chains; and

(D) analyzing the interaction of all or part of each of said amino acid side chains from said group with all or part of said protein structure to generate a set of optimized protein sequences.

Claims 54-55 (Canceled)

56. (Previously presented) A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

(A) receiving a protein structure of a desired target protein, said protein structure comprising:

i) a protein template structure comprising a protein backbone structure and at least one non-variable residue; and

ii) a plurality of variable residue positions;

(B) altering at least one supersecondary structure parameter value of the protein backbone structure of said protein;

(C) establishing a group of potential amino acid side chains for a plurality of variable residue positions of said protein, wherein at least one of said amino acid side chains is from a hydrophilic amino acid; and

(D) analyzing the interaction of all or part of each of said potential amino acid side chains from said group with all or part of said protein structure to generate a set of optimized proteins sequences, wherein said analyzing step includes the use of at least one scoring function.

57. (Previously presented) A method according to claim 56 wherein said amino acid side chains are different.

58. (Previously presented) A method according to claim 56 wherein said amino acid side chains are the same.

59. (Original) A method according to claim 56 wherein said hydrophilic amino acid is selected from the group consisting of serine, threonine, aspartic acid, asparagine, glutamine, glutamic acid, arginine, lysine, and histidine.

60. (Currently amended) A method according to claims 53 and 56-59 further comprising physically generating at least one member of said set of optimized protein sequences and experimentally testing said sequence for a desired function.

61. (Previously presented) A method according to claim 30, 31, or 53 wherein said analyzing step comprises a DEE computation.

62. (Previously presented) A method according to claim 56 wherein said analyzing step further comprises a DEE computation.

63. (Previously presented) A method according to claim 56 wherein said set of optimized protein sequences comprises the globally optimal protein sequence.

64. (Currently amended) A method according to claim 61 ~~or 62~~ wherein said DEE computation is selected from the group consisting of original DEE and Goldstein DEE.

65. (Previously presented) A method according to claim 30, 31, or 53 wherein said analyzing step includes the use of at least one scoring function.

66. (Currently amended) A method according to claim 56 ~~or 65~~ wherein said scoring function is selected from the group consisting of a van der Waals potential scoring function, a hydrogen bond potential scoring function, an atomic solvation scoring function, an electrostatic scoring function and a secondary structure propensity scoring function.

67. (Previously presented) A method according to claim 65 wherein said analyzing step includes the use of at least two scoring functions.

68. (Previously presented) A method according to claim 65 wherein said analyzing step includes the use of at least three scoring functions.

69. (Previously presented) A method according to claim 65 wherein said analyzing step includes the use of at least four scoring functions.

70. (Previously presented) A method according to claim 66 wherein said scoring function is an atomic solvation scoring function.

71. (Previously presented) A method according to claim 70 wherein said atomic solvation scoring function includes a scaling factor that compensates for over-counting.

72. (Previously presented) A method according to claim 30, 31, 53, or 56 further comprising experimentally testing at least one member of said set.

73. (Previously presented) A method according to claim 63 further comprising the step of:

generating a list of additional optimal sequences from said globally optimal protein sequence.

74. (Previously presented) A method according to claim 73 wherein said generating includes the use of a Monte Carlo search.

75. (Previously presented) A method according to claim 30, 31, 53, or 56 wherein said analyzing step comprises a Monte Carlo computation.

76. (Currently amended) A method according to claim 75 further comprising the step of: testing some or all of said protein sequences from said ~~list~~ set to produce potential energy test results.

77. (Previously presented) A method according to claim 76 further comprising the step of:

analyzing the correspondence between said potential energy test results and theoretical potential energy data.

78. (Previously presented) A method according to claim 30, 31, 53, or 56 further comprising modulating the protein backbone structure.

79. (Previously presented) A method according to claim 30, 31, 53, or 56 wherein said variable residue positions comprise one or more non-core positions.

80. (Currently Amended) ~~A method according to 53 wherein step (c) further comprises a second group for a second variable position has a second set of at least two amino acid side chains.~~ A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

(A) receiving a protein structure of a desired target protein, said protein structure comprising:

i) a protein template structure comprising a protein backbone structure and at least one non-variable residue; and

ii) a plurality of variable residue positions;

(B) altering at least one supersecondary structure parameter value of said protein backbone structure prior to establishing a group of potential amino acid side chains;

(C) establishing a group of potential amino acid side chains for each of said variable residue positions, wherein a first group for a first variable position has a first set of at least two amino acid side chains and a second group for a second variable position having a second set of at least two amino acid side chains; and

(D) analyzing the interaction of all or part of each of said amino acid side chains from said group with all or part of said protein structure to generate a set of optimized protein sequences.

81. (Currently amended) A method according to claim 80 wherein said first and second sets of amino acid side chains are different.

82. (Currently amended) A method according to claim 80 wherein said first and second sets of amino acid side chains are the same.

83. (Previously presented) A method according to 30, 31, 53 or 56, wherein said at least one non-variable residues is fixed.

84. (Previously presented) A method according to 30, 31, 53 or 56, wherein said at least one non-variable residues is floated.

85. (Previously presented) A method according to claim 30, 31, 53 or 56 wherein said variable residue positions are structurally functional residue positions.

86. (Previously presented) A method according to claim 30, 31, 53, or 56 wherein said variable residue positions are biologically functional residue positions.

87. (New) A method according to claim 62 wherein said DEE computation is selected from the group consisting of original DEE and Goldstein DEE.

88. (New) A method according to claim 62 wherein said DEE computation is selected from the group consisting of original DEE and Goldstein DEE.

## REMARKS

Claims 30, 31, 53, 56-88 are pending in this application. Claims 30, 31, 53, 56-63, 65, and 67-86 are allowed. Support for new claim 87 is found in pending claim 64. Support for new claim 88 is found in pending claim 66.

The Advisory Action states that claims 64 and 66 are objected to under 37 C.F.R. 1.75(c) as being in improper multiple dependent form. Claims 64 and 66 have been amended to reflect proper dependency. Applicants respectfully request withdrawal of the rejection under 37 C.F.R. 1.75(c).

Please direct further questions in connection with this Application to the undersigned at (415) 781-1989.

Respectfully submitted,

DORSEY & WHITNEY LLP

Dated: 4/14/04

By: _____

Four Embarcadero Center
Suite 3400
San Francisco, CA 94111-4187
Telephone: (415) 781-1989
Fax No. (415) 398-3249

Renee M. Kosslak, Reg. No. 47,717 for
Robin M. Silva, Reg. No. 38,304

***Customer No. 32940***

PTO/SB/21 (08-03)
Approved for use through 08/30/2003. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE



# TRANSMITTAL FORM

*(to be used for all correspondence after initial filing)*

| | |
|---|---|
| Application Number | 09/812,034 |
| Filing Date | March 19, 2001 |
| First Named Inventor | MAYO |
| Art Unit | 1637 |
| Examiner Name | KIM, Young J |
| Attorney Docket Number | 65353.6 |

Total Number of Pages in This Submission: 10

## ENCLOSURES *(Check all that apply)*

- [x] Fee Transmittal Form
- [x] Fee Attached
- [x] Amendment/Reply
- [x] After Final
- [ ] Affidavits/declaration(s)
- [x] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Response to Missing Parts/ Incomplete Application
- [ ] Response to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
- [ ] After Allowance communication to Technology Center (TC)
- [ ] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)
- [ ] Proprietary Information
- [ ] Status Letter
- [ ] Other Enclosure(s) (please identify below):

**Remarks**

1 page Transmittal
9 pages Amendment
1 page Petition Ext. of Time (duplicate)
1 page Fee Transmitta

## SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

| | |
|---|---|
| Firm or Individual name | Joyce L. Morrison |
| Signature | |
| Date | February 12, 2004 |

## CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P O Box 1450, Alexandria, VA 22313-1450 on the date shown below.

| | | | |
|---|---|---|---|
| Typed or printed name | Joyce L. Morrison | | |
| Signature | | Date | February 12, 2004 |

PTO/SB/22 (08-03)
Approved for use through 7/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARMENT OF COMMERCE


**PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)** | Docket Number (Optional) A-65353-6

In re Application of MAYO et al
Application Number 09/812,034 | Filed March 19, 2001
For Apparatus and Method for Automated Protein Design
Art Unit 1637 | Examiner KIM, Young J.

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application.

The requested extension and appropriate non-small-entity fee are as follows (check time period desired):

- [X] One month (37 CFR 1.17(a)(1)) $110.00
- [ ] Two months (37 CFR 1.17(a)(2)) $ _____
- [ ] Three months (37 CFR 1.17(a)(3)) $ _____
- [ ] Four months (37 CFR 1.17(a)(4)) $ _____
- [ ] Five months (37 CFR 1.17(a)(5)) $ _____

[X] Applicant claims small entity status. See 37 CFR 1.27. Therefore, the fee amount shown above is reduced by one-half, and the resulting fee is: $ 55.00.

[ ] A check in the amount of the fee is enclosed.

[ ] Payment by credit card. Form PTO-2038 is attached.

[ ] The Director has already been authorized to charge fees in this application to a Deposit Account.

[X] The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 503325.

I have enclosed a duplicate copy of this sheet.

I am the
- [ ] applicant/inventor.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed (Form PTO/SB/96).
- [X] attorney or agent of record. Registration Number 31,902
- [ ] attorney or agent under 37 CFR 1.34(a). Registration number if acting under 37 CFR 1.34(a) _____

**WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.**

February 12, 2004
Date

Signature

626-737-8019
Telephone Number

Joyce L. Morrison
Typed or printed name

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below.

[X] Total of 2 forms are submitted.

PTO/SB/22 (08-03)
Approved for use through 7/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARMENT OF COMMERCE


# PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)

Docket Number (Optional) A-65333-6



| | |
|---|---|
| In re Application of | MAYO et al |
| Application Number | 09/812,034 — Filed March 19, 2001 |
| For | Apparatus and Method for Automated Protein Design |
| Art Unit | 1637 — Examiner KIM, Young J. |

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application.

The requested extension and appropriate non-small-entity fee are as follows (check time period desired):

- [X] One month (37 CFR 1.17(a)(1)) $110.00
- [ ] Two months (37 CFR 1.17(a)(2)) $ ____
- [ ] Three months (37 CFR 1.17(a)(3)) $ ____
- [ ] Four months (37 CFR 1.17(a)(4)) $ ____
- [ ] Five months (37 CFR 1.17(a)(5)) $ ____

[X] Applicant claims small entity status. See 37 CFR 1.27. Therefore, the fee amount shown above is reduced by one-half, and the resulting fee is: $ 55.00.

- [ ] A check in the amount of the fee is enclosed.
- [ ] Payment by credit card. Form PTO-2038 is attached.
- [ ] The Director has already been authorized to charge fees in this application to a Deposit Account.
- [X] The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 502325.

I have enclosed a duplicate copy of this sheet.

I am the

- [ ] applicant/inventor.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed (Form PTO/SB/96).
- [X] attorney or agent of record. Registration Number 31,902
- [ ] attorney or agent under 37 CFR 1.34(a). Registration number if acting under 37 CFR 1.34(a) ____

**WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.**

February 12, 2004
Date

Signature

626-737-8019
Telephone Number

Joyce L. Morrison
Typed or printed name

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below.

[X] Total of 2 forms are submitted.

PTO/SB/17 (08-03)
Approved for use through 07/31/2006. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE



# FEE TRANSMITTAL for FY 2003

*Effective 01/01/2003. Patent fees are subject to annual revision.*

☑ Applicant claims small entity status. See 37 CFR 1.27

**TOTAL AMOUNT OF PAYMENT** ($) 465.00

| Complete if Known | |
|---|---|
| Application Number | 09/812,034 |
| Filing Date | March 19, 2001 |
| First Named Inventor | Mayo |
| Examiner Name | KIM, Young J. |
| Art Unit | 1637 |
| Attorney Docket No. | 65353 6 |

## METHOD OF PAYMENT *(check all that apply)*

☐ Check ☐ Credit card ☐ Money Order ☐ Other ☐ None

☑ Deposit Account:

Deposit Account Number: 502325

Deposit Account Name:

**The Director is authorized to:** *(check all that apply)*

☑ Charge fee(s) indicated below ☑ Credit any overpayments

☐ Charge any additional fee(s) during the pendency of this application

☐ Charge fee(s) indicated below, **except for the filing fee** to the above-identified deposit account.

## FEE CALCULATION

### 1. BASIC FILING FEE

| Large Entity Fee Code | Large Entity Fee ($) | Small Entity Fee Code | Small Entity Fee ($) | Fee Description | Fee Paid |
|---|---|---|---|---|---|
| 1001 | 750 | 2001 | 375 | Utility filing fee | |
| 1002 | 330 | 2002 | 165 | Design filing fee | |
| 1003 | 520 | 2003 | 260 | Plant filing fee | |
| 1004 | 750 | 2004 | 375 | Reissue filing fee | |
| 1005 | 160 | 2005 | 80 | Provisional filing fee | |

**SUBTOTAL (1)** ($)

### 2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

| | Extra Claims | | Fee from below | Fee Paid |
|---|---|---|---|---|
| Total Claims | -20** = | | x | = |
| Independent Claims | - 3** = | | x | = |
| Multiple Dependent | | | | = |

| Large Entity Fee Code | Large Entity Fee ($) | Small Entity Fee Code | Small Entity Fee ($) | Fee Description |
|---|---|---|---|---|
| 1202 | 18 | 2202 | 9 | Claims in excess of 20 |
| 1201 | 84 | 2201 | 42 | Independent claims in excess of 3 |
| 1203 | 280 | 2203 | 140 | Multiple dependent claim, if not paid |
| 1204 | 84 | 2204 | 42 | ** Reissue independent claims over original patent |
| 1205 | 18 | 2205 | 9 | ** Reissue claims in excess of 20 and over original patent |

**SUBTOTAL (2)** ($)

**or number previously paid, if greater; For Reissues, see above

## FEE CALCULATION (continued)

### 3. ADDITIONAL FEES

| Large Entity Fee Code | Large Entity Fee ($) | Small Entity Fee Code | Small Entity Fee ($) | Fee Description | Fee Paid |
|---|---|---|---|---|---|
| 1051 | 130 | 2051 | 65 | Surcharge - late filing fee or oath | |
| 1052 | 50 | 2052 | 25 | Surcharge - late provisional filing fee or cover sheet | |
| 1053 | 130 | 1053 | 130 | Non-English specification | |
| 1812 | 2,520 | 1812 | 2,520 | For filing a request for *ex parte* reexamination | |
| 1804 | 920* | 1804 | 920* | Requesting publication of SIR prior to Examiner action | |
| 1805 | 1,840* | 1805 | 1,840* | Requesting publication of SIR after Examiner action | |
| 1251 | 110 | 2251 | 55 | Extension for reply within first month | 55.00 |
| 1252 | 410 | 2252 | 205 | Extension for reply within second month | |
| 1253 | 930 | 2253 | 465 | Extension for reply within third month | |
| 1254 | 1,450 | 2254 | 725 | Extension for reply within fourth month | |
| 1255 | 1,970 | 2255 | 985 | Extension for reply within fifth month | |
| 1401 | 320 | 2401 | 160 | Notice of Appeal | |
| 1402 | 320 | 2402 | 160 | Filing a brief in support of an appeal | |
| 1403 | 280 | 2403 | 140 | Request for oral hearing | |
| 1451 | 1,510 | 1451 | 1,510 | Petition to institute a public use proceeding | |
| 1452 | 110 | 2452 | 55 | Petition to revive - unavoidable | |
| 1453 | 1,300 | 2453 | 650 | Petition to revive - unintentional | |
| 1501 | 1,300 | 2501 | 650 | Utility issue fee (or reissue) | |
| 1502 | 470 | 2502 | 235 | Design issue fee | |
| 1503 | 630 | 2503 | 315 | Plant issue fee | |
| 1460 | 130 | 1460 | 130 | Petitions to the Commissioner | |
| 1807 | 50 | 1807 | 50 | Processing fee under 37 CFR 1.17(q) | |
| 1806 | 180 | 1806 | 180 | Submission of Information Disclosure Stmt | |
| 8021 | 40 | 8021 | 40 | Recording each patent assignment per property (times number of properties) | |
| 1809 | 750 | 2809 | 375 | Filing a submission after final rejection (37 CFR 1.129(a)) | |
| 1810 | 750 | 2810 | 375 | For each additional invention to be examined (37 CFR 1.129(b)) | |
| 1801 | 750 | 2801 | 375 | Request for Continued Examination (RCE) | |
| 1802 | 900 | 1802 | 900 | Request for expedited examination of a design application | |

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid

**SUBTOTAL (3)** ($) 55.00

## SUBMITTED BY

| | | | | | |
|---|---|---|---|---|---|
| Name (Print/Type) | Joyce L. Morrison | Registration No. (Attorney/Agent) | 31,902 | Telephone | (626) 737-801 |
| Signature | | | | Date | February 12, 2004 |

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PATENT
Attorney Docket No. A-65353-6/RFT/RMS/RMK

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of

MAYO, *et al.*

Serial No. 09/812,034

Filed: March 19, 2001

For: *Apparatus and Method for Automated Protein Design*

Group No. 1637

Examiner: Kim, Young J.

**CERTIFICATE OF FACSIMILE TRANSMISSION**

I hereby certify that this correspondence, included listed enclosures, is being facsimile transmitted to the United States Patent and Trademark Office, Fax No. (703) 872-9306 on February 12, 2004.

Signature: _____
Joyce L. Morrison

**AMENDMENT AND RESPONSE AFTER FINAL OFFICE ACTION**

Assistant Commissioner for Patents
Alexandria, VA 22313

Sir:

This paper is being submitted in response to the Office Action mailed October 15, 2003 and the Advisory Action mailed January 6, 2004. This response is filed on or before the due date of February 15, 2004, with a petition for a one-month extension of time, and appropriate fees. The Commissioner is authorized to charge any additional fees, including any extension fees, which may be required, or credit any overpayment to Deposit Account No. 502325.

Claims Listing begins on page 2
Remarks begin on page 8

**Claims Listing:**

Claims 1 -29 (Canceled)

30. (Previously Amended) A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

(A) receiving a protein structure of a desired target protein, said protein structure comprising:;

i) a protein template structure comprising a protein backbone structure and at least one non-variable residue; and

ii) a plurality of variable residue positions;

(B) altering at least one supersecondary structure parameter value of said protein backbone structure of said protein;

(C) establishing a group of potential amino acid side chains for a plurality of said variable residue positions of said protein; and

(D) analyzing the interaction of all or part of each of said potential amino acid side chains from said group with all or part of the remainder of said protein structure to generate a set of optimized proteins sequences.

31. (Currently Amended) A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

(A) receiving a protein structure of a desired target protein, said protein structure comprising:

i) a protein template structure comprising a protein backbone structure and at least one non-variable residue; and

ii) a plurality of variable residue positions;

(B) altering at least one supersecondary structure parameter value of said protein backbone structure;

(C) classifying each variable residue position as either a core, surface or boundary residue;

(D) establishing a group of potential amino acid side chains for each of said variable residue positions; and

(E) analyzing the interaction of all or part of each of said amino acid side chains from said group with all or part of ef said protein structure to generate a set of optimized protein sequences.

32. (Previously Canceled)
33. (Previously Canceled)
34. (Previously Canceled)
35. (Previously Canceled)
36. (Previously Canceled)
37. (Previously Canceled)
38. (Previously Canceled)
39. (Previously Canceled)
40. (Previously Canceled)
41. (Previously Canceled)
42. (Previously Canceled)
43. (Previously Canceled)
44. (Previously Canceled)
45. (Previously Canceled)
46. (Previously Canceled)
47. (Previously Canceled)
48. (Previously Canceled)
49. (Previously Canceled)
50. (Previously Canceled)
51. (Previously Canceled)
52. (Previously Canceled)

53. (Previously Amended) A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

(A) receiving a protein structure of a desired target protein, said protein structure comprising:

i) a protein template structure comprising a protein backbone structure and at least one non-variable residue; and

ii) a plurality of variable residue positions;

(B) altering at least one supersecondary structure parameter value of said protein backbone structure prior to establishing a group of potential amino acid side chains;

(C) establishing a group of potential amino acid side chains for each of said variable residue positions, wherein a first group for a first variable position has a first set of at least two amino acid side chains; and

(D) analyzing the interaction of all or part of each of said amino acid side chains from said group with all or part of said protein structure to generate a set of optimized protein sequences.

54. (Previously Canceled)

55. (Previously Canceled)

56. (Previously Amended) A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

(A) receiving a protein structure of a desired target protein, said protein structure comprising:

i) a protein template structure comprising a protein backbone structure and at least one non-variable residue; and

ii) a plurality of variable residue positions;

(B) altering at least one supersecondary structure parameter value of the protein backbone structure of said protein;

(C) establishing a group of potential amino acid side chains for a plurality of variable residue positions of said protein, wherein at least one of said amino acid side chains is from a hydrophilic amino acid; and

(D) analyzing the interaction of all or part of each of said potential amino acid side chains from said group with all or part of said protein structure to generate a set of optimized proteins sequences, wherein said analyzing step includes the use of at least one scoring function.

57. (Previously Amended) A method according to claim 56 wherein said amino acid side chains are different.

58. (Previously Amended) A method according to claim 56 wherein said amino acid side chains are the same.

59. (Original) A method according to claim 56 wherein said hydrophilic amino acid is selected from the group consisting of serine, threonine, aspartic acid, asparagine, glutamine, glutamic acid, arginine, lysine, and histidine.

60. (Currently Amended) A method according to claims 53 and 56-59 further comprising physically generating at least one member of said set of optimized protein sequences and experimentally testing said sequence for a desired function.

61. (Previously Added) A method according to claim 30, 31, or 53 wherein said analyzing step comprises a DEE computation.

62. (Previously Added) A method according to claim 56 wherein said analyzing step further comprises a DEE computation.

63. (Previously Added) A method according to claim 56 wherein said set of optimized protein sequences comprises the globally optimal protein sequence.

64. (Previously Added) A method according to claim 61 or 62 wherein said DEE computation is selected from the group consisting of original DEE and Goldstein DEE.

65. (Previously Added) A method according to claim 30, 31, or 53 wherein said analyzing step includes the use of at least one scoring function.

66. (Previously Added) A method according to claim 56 or 65 wherein said scoring function is selected from the group consisting of a van der Waals potential scoring function, a hydrogen bond potential scoring function, an atomic solvation scoring function, an electrostatic scoring function and a secondary structure propensity scoring function.

67. (Previously Added) A method according to claim 65 wherein said analyzing step includes the use of at least two scoring functions.

68. (Previously Added) A method according to claim 65 wherein said analyzing step includes the use of at least three scoring functions.

69. (Previously Added) A method according to claim 65 wherein said analyzing step includes the use of at least four scoring functions.

70. (Previously Added) A method according to claim 66 wherein said scoring function is an atomic solvation scoring function.

71. (Previously Added) A method according to claim 70 wherein said atomic solvation scoring function includes a scaling factor that compensates for over-counting.

72. (Previously Added) A method according to claim 30, 31, 53, or 56 further comprising experimentally testing at least one member of said set.

73. (Previously Added) A method according to claim 63 further comprising the step of:

generating a list of additional optimal sequences from said globally optimal protein sequence.

74. (Previously Added) A method according to claim 73 wherein said generating includes the use of a Monte Carlo search.

75. (Previously Added) A method according to claim 30, 31, 53, or 56 wherein said analyzing step comprises a Monte Carlo computation.

76. (Currently Amended) A method according to claim 75 further comprising the step of: testing some or all of said protein sequences from said ~~list~~ set to produce potential energy test results.

77. (Previously Added) A method according to claim 76 further comprising the step of: analyzing the correspondence between said potential energy test results and theoretical potential energy data.

78. (Previously Added) A method according to claim 30, 31, 53, or 56 further comprising modulating the protein backbone structure.

79. (Previously Added) A method according to claim 30, 31, 53, or 56 wherein said variable residue positions comprise one or more non-core positions.

80. (Currently Amended) ~~A method according to 53 wherein~~ step ~~(c) further comprises a second group for a second variable position has a second set of at least two amino acid side chains.~~ A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

(A) receiving a protein structure of a desired target protein, said protein structure comprising:

i) a protein template structure comprising a protein backbone structure and at least one non-variable residue; and

ii) a plurality of variable residue positions;

(B) altering at least one supersecondary structure parameter value of said protein backbone structure prior to establishing a group of potential amino acid side chains;

(C) establishing a group of potential amino acid side chains for each of said variable residue positions, wherein a first group for a first variable position has a first set of at least two amino acid side chains and a second group for a second variable position having a second set of at least two amino acid side chains; and

(D) analyzing the interaction of all or part of each of said amino acid side chains from said group with all or part of said protein structure to generate a set of optimized protein sequences.

81. (Currently Amended) A method according to claim 80 wherein said first and second sets of amino acid side chains are different.

82. (Currently Amended) A method according to claim 80 wherein said first and second sets of amino acid side chains are the same.

83. (Previously Added) A method according to 30, 31, 53 or 56, wherein said at least one non-variable residues is fixed.

84. (Previously Added) A method according to 30, 31, 53 or 56, wherein said at least one non-variable residues is floated.

85. (Previously Added) A method according to claim 30, 31, 53 or 56 wherein said variable residue positions are structurally functional residue positions.

86. (Previously Added) A method according to claim 30, 31, 53, or 56 wherein said variable residue positions are biologically functional residue positions.

## REMARKS

Claims 30, 31, 53, 56-86 are pending in this application. Claims 30, 31, 53, 56-79 and 83-86 are allowed. Claims 76-78 and 80-82 are rejected. Claim 31 has been amended to correct a typographical error. Claim 60 has been amended to reflect proper dependency.

**Rejection under 35 U.S.C.§ 112, first paragraph**

Claim 78 is rejected under 35 U.S.C.§ 112, first paragraph, as failing to comply with the written description requirement because the specification provides no support for such a limitation. Applicants submit that the backbone, involved in the optimization, may be modulated either rationally or manually. Applicant respectfully points to support in the Specification at beginning on page 10, line 9 through page 11, line 16 and page 13, lines 21-33, and that a person skilled in the art would understand tho Applicants to have been in possession of the claimed invention at the time the application was filed. Applicants submit that no new matter has been added by the amendment. Applicant respectfully requests the reconsideration and withdrawal of the rejection of Claim 78, in light of the foregoing argument.

**Rejection under 35 U.S.C.§ 112, second paragraph**

Claims 76, 77, and 80-82 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter of the present invention. Claim 76 has been amended to recite, "said set" instead of "said list." The antecedent basis has been corrected by this Amendment thereby making Claim 76 and its dependent claim 77 definite and more clearly describing the claimed invention.

Claim 80 was rejected as being indefinite for reciting "wherein step (c) comprises a second group for a second variable position has a second set of at least two amino acid side chains." Claim 80 has been amended into independent form, now including the allowed original base claim that it depended from. Support for the amendment may be found in allowed claim 53 and claim 80 as originally filed and in the Specification at page 7, lines 18-26 and page 10, lines 5-30and page 11, lines 9-16, page 14, lines 14-21 and page 18, lines 1-19.

Claims 81 and 82 have been amended to recite "said first and second sets of amino acid side chains," to reflect proper antecedent basis and the clarify the claim language.

USSN: 09/812,034
Filing Date: March 19, 2001

Accordingly, Applicants respectfully request the reconsideration and withdrawal of the rejection of Claims 76, 77, and 80-82 under 35 U.S.C. § 112, second paragraph, in light of the-above amendmonts.

The Applicants submit that in light of the above-amendment and argument, the claims are now in condition for allowance and an early notification of such is respectfully solicited.

Please direct any calls in connection with this application to the undersigned at (626) 737-8019.

Dated: February 12, 2004
Customer Number: 33315
Xencor
111 W. Lemon Avenue
Monrovia, California 91016
Phone: 626-737-8019
Fax: 626-256-3760

Respectfully submitted,

By: _____
Joyce L. Morrison, Reg. No. 31,902

[redacted]

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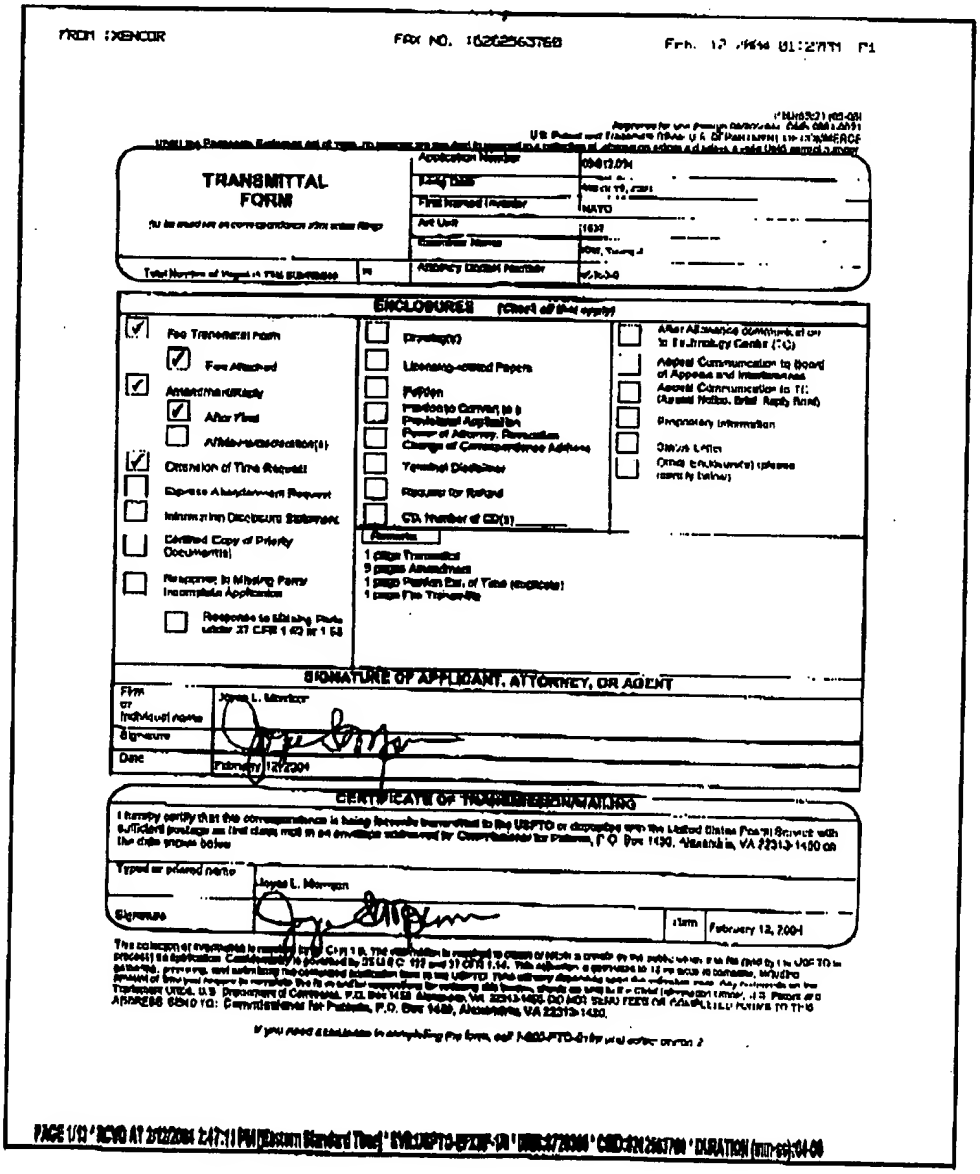

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Firm or Individual name: Joyce L. Morrison
Signature:
Date: February 12, 2004

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